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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,489	12/05/2001	Elizabeth Gay Frayne		2256

7590 08/09/2005
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EXAMINER

KHARE, DEVESH

ART UNIT PAPER NUMBER

1623

DATE MAILED: 08/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/007,489

Applicant(s)

FRAYNE, ELIZABETH GAY

Examiner

Devesh Khare

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

The applicant's remarks received on 04/25/2005 have been entered in view of the RCE request. The notice of non-compliance dated 5/09/2005 has been addressed and corrected by the applicant's response dated 5/20/2005. Claims 1,3,4 and 5 have been amended. Claim 6 has been cancelled.

During the course of reconsideration of the application, a prior art reference not previously disclosed by the applicants or the examiner came to light (see rejection below).

Claims 1-5 are currently pending in this application.

Minor objections

1. Claims 1-5 are objected to because of the following informalities:

In claims 1-5, the use of term "process" or "method" is not consistent.

Appropriate correction is required.

35 U.S.C. 112, second paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under the second paragraph of 35 U.S.C. 112, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A) Claims 2 and 3 provide for the use of phosphorothioate to generate nucleic acids in vivo, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

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(B) In claims 1 and 5, the phrases "such that" or "such as" render the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims which depend from an indefinite claim which fail to obviate the indefiniteness of the claim from which they depend are also seen to be indefinite and are also rejected for the reasons set forth supra.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2 and 3 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 1- 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sayers et al. (Sayers) (Directed Mutagen. 49-69, 1991) in view of Nikiforov et al (Nikiforov) (U.S. Patent 5,518,900).

Claims 1-5 are drawn to a process of generating phosphorothioate substituted nucleic acids *in vivo* comprising:

Preparing microbial culture depleted in phosphate and adding thiophosphate to the media which enables the synthesis of phosphorothioate nucleotide.

Dependent claim limitations include phosphorothioate ds DNA, ss RNA and/or RNA; cells are of eukaryotic origin; and source of phosphate is a derivative of thiophosphate such as dithiophosphate or methylthiophosphate.

Sayers teaches the phosphorothioate-based oligonucleotide directed mutagenesis method for repairing the DNA *in vitro* (see page 49, Intro. 3rd. para.). Sayers discloses that a phosphorothioate group may be incorporated exclusively into the strand of a newly synthesized RF-IV DNA in a cell (page 50, first para. and Figure 1). Sayer also discloses the phosphorylation of the mismatch primer wherein the phosphorylation is catalysed by the enzyme polynucleotide kinase and requires ATP and the said phosphorylated primer is then combined with the template DNA (see page 55, 2nd para. Preparation of RF-IV DNA). While the Sayers's method of generating phosphorothioate oligo mixtures is closely analogous to the applicant's method, Sayers's method of generating phosphorothioate oligo mixtures differ from applicant's method that the process steps of claim 1 are not specifically disclosed.

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Nikiforov teaches a method to generate phosphorothioate derivatives of single stranded DNA molecules (col. 4, lines 55-65). Nikiforov discloses the process steps for generating phosphorothioate substituted single-stranded DNA by the incubating the phosphorothioated primer to generate the phosphorothioate single-stranded DNA (col. 7, lines 30-50). Nikiforov also discloses the phosphorothioated DNA and RNA (col. 14, lines 10-20).

It would have been obvious to person having ordinary skill in the art at the time the invention was made, to modify the method of generating phosphorothioate substituted nucleic acids in a cell as taught by Sayers in combination with the process steps to generate phosphorothioate derivatives of single stranded DNA molecules of Nikiforov. The motivation is provided by the Sayers reference, Sayers discloses that certain restriction endonucleases are incapable of hydrolyzing phosphorothioate internucleotide linkages therefore the phosphorothioate containing oligonucleotides can be protected from degradation in vivo (page 50, 1st para.).

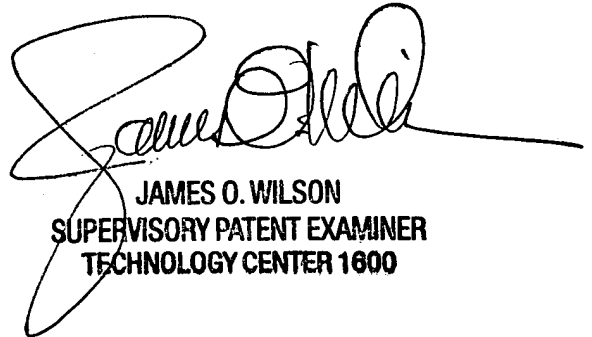
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Devesh Khare whose telephone number is 571-272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be

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reached at 571-272-0661. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,JD.
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August 5,2005



JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600